CLINICAL CASE

Contralateral ureteral metastasis due to clear cell renal tumor

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PALABRAS CLAVE
Carcinoma renal; Metástasis; Inmunohistoquímica

Abstract
Renal cell carcinoma represents 2-3% of all cancers and is the most frequent solid lesion of the kidney. Incidental diagnosis through imaging studies is approximately 50%, and the majority of those cases are asymptomatic. Management is based on radical surgical treatment and postoperative follow-up through imaging techniques is essential for detecting local or systemic recurrence.

A 60-year-old man had a past history of left radical nephrectomy due to renal tumor 10 years earlier. Clinical manifestation was painless, gross hematuria. CT-urography revealed right ureteropelvic ectasia with a lesion occupying the distal third of the ureter that produced a negative filling defect. Endoscopic revision, lesion excision, and adjuvant treatment based on the tyrosine kinase inhibitor, sorafenib, were carried out.

This clinical case underlines the importance of strict follow-up in patients with renal tumors since there is no clear knowledge as to the metastatic behavior and predictable tumor dissemination routes in renal cell carcinoma.

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Metástasis ureteral contralateral por tumor renal de células claras

Resumen
El carcinoma renal representa el 2-3% de todos los cánceres y es la lesión sólida más frecuente del riñón. El diagnóstico incidental por medio de pruebas de imagen es de aproximadamente el 50%. La mayoría de los casos son asintomáticos. El tratamiento quirúrgico radical es la base del manejo y el seguimiento posterior mediante técnicas de imagen es prioritario para detectar recidivas locales o sistémicas.

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Contralateral ureteral metastasis due to clear cell renal tumor

Paciente masculino de 60 años de edad, con antecedente de nefrectomía radical izquierda 10 años antes por tumor renal. La manifestación clínica es hematuria macroscópica indolora.
Se realiza UROTAC en la cual se observa ureteropielectasia derecha con lesión ocupante de uréter en tercio distal, que genera defecto de llenado negativo. Se realiza revisión endoscópica, escisión de la lesión y adyuvancia a base de inhibidor de tirosin cinasa (sorafenib).

En este caso clínico destaca la importancia del seguimiento estrecho en pacientes con neoplasias renales ante la ausencia de conocimientos claros sobre el comportamiento metastásico y las rutas de diseminación tumoral predecibles en carcinoma de células renales.

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Introduction

Renal cell carcinoma (RCC) has the capacity to metastasize to multiple organs. The most common sites include the lung, lymph nodes, bone, and liver. Metastasis in abdominopelvic organs is uncommon and it is identified through necessary radiographic support.

Other infrequent metastatic sites of RCC have been reported (table 1), underlining its unclear manner of dissemination. Pelvic organ metastasis is generally secondary to RCCs originating on the left side, supporting the idea of the venous route as the dissemination pathway.1-5

Case presentation

A 60-year-old man came to the emergency department with symptoms of painless gross hematuria with no clotting. Anamnesis revealed that he underwent left radical nephrectomy due to a kidney tumor and the histopathology study reported a 9 cm tumor with central necrosis that invaded the renal capsule. The patient did not go to the follow-up appointments after his surgery. Physical examination identified the abdominal scar from the left lumbotomy. There were no signs of visceromegaly or painful points. The laboratory work-up reported: hemoglobin 16 g/dl, platelets 167,000, creatinine 1 mg/dl, TB 1.65mg/dl, DB 0.5 mg/dl, IB 1.07mg/dl, and alkaline phosphatase 134 U/l. Non-contrast and contrast-enhanced tomography scans revealed the surgical absence of the left kidney, right ureteropelvic ectasia with a rounded lesion, 2 x 2 cm in diameter, occupying the right ureter at the level of the iliac vessel intersection. It had a density of 10-20 HU and was enhanced to 50-60 HU in the contrasted phase (figs. 1 and 2).

Table 1 Atypical metastatic sites of RCC

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<tr>
<td>Intestine</td>
<td>Saitoh, 19811</td>
</tr>
<tr>
<td>Skin</td>
<td>García Torrelles et al., 20072</td>
</tr>
<tr>
<td>Vagina</td>
<td>Osorio et al., 20082</td>
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<tr>
<td>Mouth</td>
<td>Zhang et al., 20144</td>
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<td>Thyroid</td>
<td>Medad et al., 20134</td>
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Given the tomographic evidence of the tumor lesion, ureteroscopy, biopsy, and tumor resection were performed (fig. 3).

Histopathology report: clear cell carcinoma, dysplastic epithelium, and fibrosis (fig. 4). Immunohistochemistry study was positive for CD10 and vimentin. There was little...
Ureteroscopy: hypervascularized, hyperemic, and rounded right ureteral tumor.

Photomicrography (H & E, x20): large, rounded, polygonal cells with ample clear cytoplasm and barely evident central nucleus and nucleolus, corresponding to clear cell renal cell carcinoma metastasis.

Immunohistochemical study for vimentin (x20). Intense, diffuse cytoplasmic positivity is observed (black arrow). The urothelium to the right of the image does not express vimentin (white arrow).

Immunohistochemical study with p63 (x20). Intense positivity is observed in the nuclei of the urothelial cells (white arrow), but there is tenuous and focal expression in the neoplastic cells of the subepithelial connective tissue (black arrow).

Clinical manifestation is recurrent gross hematuria. The mechanism of metastatic dissemination is unknown. However, endoluminal, hematic, and lymphatic dissemination are postulated.\textsuperscript{10} Immunohistochemical analysis of metastases essentially consists of studying the presence of intermediate filaments of cytokeratin in the tumor cells.

When renal tumors present with unusual morphologies or distinct histologic patterns, the immunohistochemical stains are of the utmost importance for the differential diagnosis.

An a mesenchymal marker, vimentin is expressed in the majority of types (87 to 100%) of conventional and papillary clear cell renal cell carcinoma.\textsuperscript{11} Expression for p63 in the cytokeratin profile, ruling out an epithelial origin of the lesion (figs. 5 and 6).

Based on the histopathologic and immunohistochemistry results, the decision was made to initiate adjuvant therapy with oral sorafenib 400 mg every 12 h for 2 months. The patient had favorable therapeutic progression with no tomographic evidence of tumor recurrence.

Discussion

RCC can extend into the renal pelvis and ipsilateral ureter,\textsuperscript{6-7} but there are few reports of metastasis to the contralateral ureter after radical nephrectomy.\textsuperscript{8-9} The most common clinical manifestation is recurrent gross hematuria. The mechanism of metastatic dissemination is unknown. However, endoluminal, hematic, and lymphatic dissemination are postulated.\textsuperscript{10}

Immunohistochemical analysis of metastases essentially consists of studying the presence of intermediate filaments of cytokeratin in the tumor cells.

When renal tumors present with unusual morphologies or distinct histologic patterns, the immunohistochemical stains are of the utmost importance for the differential diagnosis.

An a mesenchymal marker, vimentin is expressed in the majority of types (87 to 100%) of conventional and papillary clear cell renal cell carcinoma.\textsuperscript{11}
CD 10 can be useful in diagnosing RCC, but it does not confirm the diagnosis, given that CD 10 is present in multiple neoplasias.\textsuperscript{12}

The marker p63 is expressed in high percentages of urothelial neoplasias, but it is not expressed in renal cell carcinoma, therefore it is useful in the differential diagnosis of neoplasias of epithelial origin.\textsuperscript{13}

Metastatic RCC resection through ureterectomy, radical nephrectomy, or the conservative endourologic technique improves long-term survival in 59 and 31\% at 3 and 5 years, respectively.\textsuperscript{14,15} Our patient underwent endourologic resection to avoid the need for later dialysis that would increase morbidity and mortality.

Sorafenib is a potent inhibitor of kinases and the VEGF in vitro and has a great cytostatic capacity. We administered it to our patient with good clinical response and subsequent radiographic results.

**Conclusions**

Given the unpredictable metastatic dissemination of RCC, strict postoperative clinical and radiographic follow-up is of the utmost importance in the search for surgical site metastasis, distant metastasis, and metastasis to the rest of the urinary system. When there is evidence of tumor recurrence, immunohistochemistry studies are essential for correct diagnosis and management.

**Ethical responsibilities**

Protection of persons and animals. The authors declare that the procedures followed conformed to the ethical standards of the responsible committee on human experimentation and were in accordance with the World Medical Association and the Declaration of Helsinki.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

**Financial disclosure**

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**Conflict of interest**

The authors declare that there is no conflict of interest.

**References**